

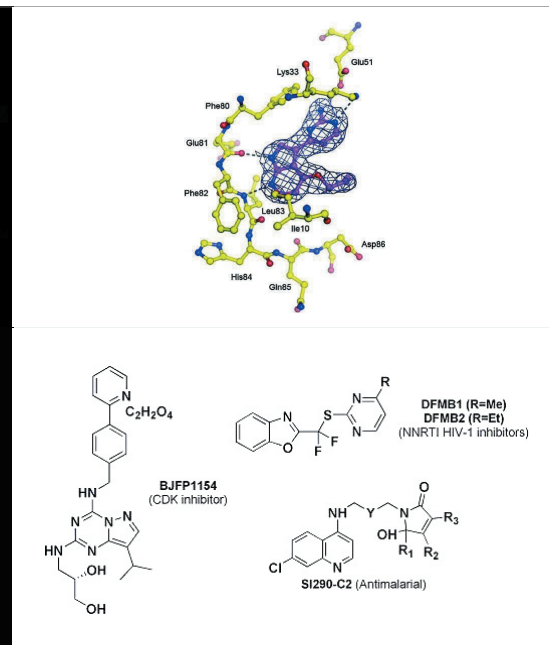
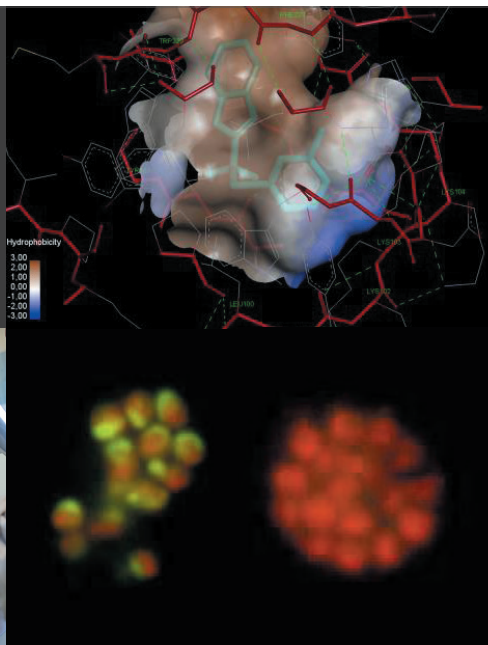
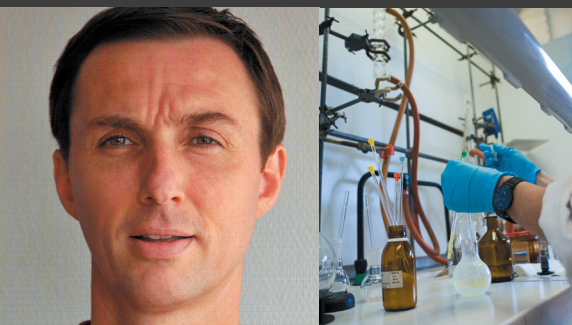
| GROUP

## DRUG DISCOVERY AND MEDICINAL CHEMISTRY (SMITH)

ICBMS - UMR 5246, UNIVERSITÉ CLAUDE BERNARD LYON 1 – CNRS - INSA LYON – CPE LYON

BENOIT  
JOSEPH

Professor



**Organic synthesis towards the development of new chemotherapeutic agents to treat cancer, infectious and neurodegenerative diseases is the mainstream of our laboratory. The aim of the team is to provide chemical and biological solutions to these issues, from drug design to the understanding of their mechanism of action.**

### TOPICS

Methodologies in heterocyclic chemistry  
– Drug candidates – Fluorine chemistry –  
Electrochemistry – Malaria – Mycology

### MEDICINAL CHEMISTRY

Drug candidates are elaborated to treat human pathologies such as cancer, malaria, aids or neurodegenerative diseases. Pharmacological tools have been designed to investigate human or parasitic biological processes (apoptosis, resistance, ischemia, VIH transcription,...).

Research challenges include:

- Selective CMGC kinase inhibitors (CDKs, CLKs, Dyrks, CK1 and GSK3)
- New antimalarial drug design
- Non Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
- Metal complexes as metallodrugs

- Serotonergic ligands
- Anticancer agents

### FLUORINE CHEMISTRY

New methodologies are developed to introduce fluorine atoms as well as difluoromethylene, or trifluoromethyl moieties into organic molecules of synthetic and biological significance.

Research challenges include:

- Redox catalytic transformations to create C-C, C-N, C-O and C-S bonds
- Novel fluoroalkylated ligands and their metal complexes for catalysis, therapeutic and materials applications
- Novel approaches to fluoro and gem-difluoro nucleosides
- Photoredox catalysis

### MALARIA

Artemisinin-based combined therapy (ACTs) and climatic changes have transformed the global impact of malaria in endemic areas; this parasitic disease remains a major life-threatening challenge for millions of people.

Research challenges include:

- Deciphering the mechanism of action of new antimalarial drugs
- Knowledge breakthrough on apoptosis role in anti-parasitic diseases
- Pre-clinical studies of antiparasitic and antifungal drugs
- Clinical phase I-II-III clinical studies in endemic areas

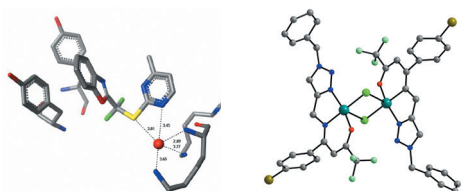
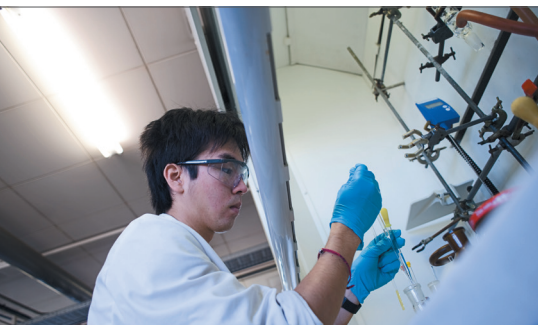
### | Figures

*Centre, top: Docking of a DFMB1 (NNRTI) with Reverse Transcriptase.*

*Center, bottom: Plasmodium falciparum schizontes: polarized mitochondria (left), DNA binding (right).*

*Right, top: Cocrystal structure of meriolin 5 bound to CDK2/cyclin A.*

*Right, bottom: Lead compounds (BJFP1154, DFMB1, DFMB2, SI290-C2).*

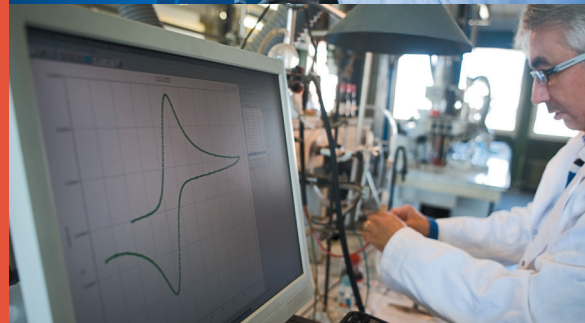
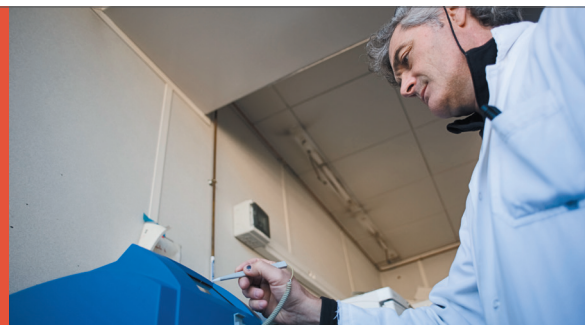


#### | EQUIPMENT

- › Biotage Microwave
- › Potentiostat/Galvanostat PAR 263A
- › AC/DC suppliers
- › Real-time PCR
- › Animal facilities
- › L2-L3 safety level culture facilities

#### | EXPERTISES

- › Medicinal chemistry
- › Heterocyclic chemistry
- › Fluorine chemistry
- › Electrochemistry
- › Malaria
- › Parasitology and Mycology
- › Clinical trials



## COLLABORATIONS

The team has partnerships with pharmaceutical companies and start-ups: Janssen Cilag, ManRos Therapeutics, CovalAb, Gilead, Biomérieux as well as with national and international academic teams: LMI, UMR 5615 (Lyon 1); BMSSI, UMR 5086 (Lyon 1); CRNL (Lyon 1); IRCOF, UMR COBRA 6014 (Rouen); ICR, UMR 7273 (Marseille); UMR 8601 (Paris Descartes); ICOA, UMR 6005 (Orléans); UMR S 945 (INSERM/Pierre Marie Curie); DC2N (Rouen); Univ. Florida (Miami); Univ. Oxford; The Beatson Institute for Cancer Research (Glasgow); NCBID, George Mason Univ. (Manassas); New Jersey Medical School (Newark); Rega Institute for Medical Research (Leuven); Keele Univ. Staffordshire; Univ. Lausanne; Univ. Bamako; Instituto Superiore de Sanita (Rome).

## KEYWORDS

Medicinal chemistry - Fluorine chemistry - Heterocyclic chemistry - Electrochemistry - Drug candidates - Pharmacological tools - Kinase inhibitors - HIV-1 inhibitors - Malaria - Parasitology - Mycology - Preclinical and clinical trials.

## STAFF

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1-2 Post-Docs  
 2-3 PhD Students  
 2-4 Undergraduate Students

#### | Figures

*Left: Cocrystal structure of DFMB1 bound to Reverse Transcriptase (left). X-ray structure of CN198 (antimalarial) (right).*

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